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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/574,819	05/19/2000	Frank P. Luyten	NIH0099.001C1	1648

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EXAMINER

ROMEO, DAVID S

ART UNIT PAPER NUMBER

1647

DATE MAILED: 08/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/574,819	Applicant(s) LUYTEN ET AL.	
	Examiner David S Romeo	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/12/2004 has been entered.

Claims 27-32 are pending and being examined.

Maintained Formal Matters, Objections, and/or Rejections:***Claim Rejections - 35 USC § 102***

Claim 27 is rejected under 35 U.S.C. 102(a) as being anticipated by Storm (38, cited by Applicants).

Applicants submit a declaration to swear behind Storm. This declaration is ineffective to overcome the Storm reference for the reasons discussed below.

Claim Rejections - 35 USC § 103

Claims 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Storm (38, cited by Applicants) and Neidhardt (9, cited by Applicants).

Applicants argue that the Rule 131 declaration antedates the date of the Storm reference, that Neidhardt's description does not render the invention obvious because a protein comprising SEQ ID NO: 24 was unknown, and that the secondary reference does

Art Unit: 1647

not fill the gap left by antedating the primary reference. Applicant's arguments have been fully considered but they are not persuasive. This declaration is ineffective to overcome the Storm reference for the reasons discussed below. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references.

Response to Amendment

The declaration filed on 07/12/2004 under 37 CFR 1.131 has been considered but is ineffective to overcome the Storm reference.

The present claims are directed to polynucleotides encoding a genus of polypeptides comprising the amino acid sequence of SEQ ID NO: 24. The declaration is provided to evince possession of a species within the genus of polypeptides prior to the date of the Storm reference. The only species in the declaration that is encompassed by the genus of polypeptides encoded by the claimed nucleic acid molecules is the "bmp3xmatORF" species in Exhibit B attached to the declaration. It is noted that the "bmp3xmatORF" is a species that is different from the GDF-6 species disclosed by Storm. Proof of prior completion of a species different from the species of the reference or activity will be sufficient to overcome a reference indirectly under 37 CFR 1.131 if the species shown in the reference or activity would have been obvious in view of the species shown to have been made by the applicant. In re Clarke, 356 F.2d 987, 148 USPQ 665 (CCPA 1966); In re Plumb, 470 F.2d 1403, 176 USPQ 323 (CCPA 1973); In re Hostettler, 356 F.2d 562, 148 USPQ 514 (CCPA 1966). Alternatively, if the applicant

Art Unit: 1647

cannot show possession of the species of the reference or activity in this manner, the applicant may be able to antedate the reference or activity indirectly by, for example, showing prior completion of one or more species which put him or her in possession of the claimed genus prior to the reference's or activity's date. The test is whether the species completed by applicant prior to the reference date or the activity's date provided an adequate basis for inferring that the invention has generic applicability. In *re Plumb*, 470 F.2d 1403, 176 USPQ 323 (CCPA 1973); In *re Rainer*, 390 F.2d 771, 156 USPQ 334 (CCPA 1968); In *re Clarke*, 356 F.2d 987, 148 USPQ 665 (CCPA 1966); In *re Shokal*, 242 F.2d 771, 113 USPQ 283 (CCPA 1957). It is not necessary for the affidavit evidence to show that the applicant viewed his or her invention as encompassing more than the species actually made. The test is whether the facts set out in the affidavit are such as would persuade one skilled in the art that the applicant possessed so much of the invention as is shown in the reference or activity. In *re Schaub*, 537 F.2d 509, 190 USPQ 324 (CCPA 1976). The facts set out in the present declaration do not show the GDF-6 species shown in the Storm reference would have been obvious in view of the bmp3xmatORF species shown to have been made by the applicant. The declaration does not show prior completion of one or more species which put Applicants' in possession of the claimed polynucleotides encoding the genus prior to the Storm reference's date. The declaration does not provide any evidence that the bmp3xmatORF species completed by applicant prior to the Storm reference date provided an adequate basis for inferring that the invention has generic applicability. Accordingly, the facts set out in the declaration do not provide any evidence that one skilled in the art would be persuaded that applicants possessed so much of the invention as is shown in the Storm reference.

New Formal Matters, Objections, and/or Rejections:***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

5 The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10 Claims 27-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

15 The claims are directed to encompass an isolated nucleic acid molecule encoding a protein of the TGF- β family, wherein said protein comprises the amino acid sequence of SEQ ID NO: 24.

The following passages of the specification seem most relevant for construing the term "a protein of the TGF- β family:"

20 The present specification discloses that bone morphogenetic proteins (BMPs) are members of the TGF- β superfamily that can induce endochondral bone formation in adult animals. This superfamily includes a large group of structurally related signaling proteins that are secreted as dimers and then cleaved to result in biologically active carboxy terminal domains of the proteins. These bioactive proteins are characterized by 7 highly conserved cysteine residues. See page 1,
25 lines 7-11.

30 Two novel members of the TGF- β superfamily were identified and designated Cartilage-Derived Morphogenetic Protein-1 (CDMP- 1), and -2 (CDMP-2). The C-terminal TGF- β domains of these proteins were 82% identical, thus defining a novel subfamily most closely related to BMP-5, BMP-6 and osteogenic protein-1. See page 5, lines 4-7.

Art Unit: 1647

5 The nucleotide sequence and the translation of the open reading frame of CDMP-1 are presented in Figure 1. The CDMP-1 protein was predicted to have 500 amino acids, to consist of a pro-region of 376 amino acids, a typical cleavage site (Arg-Xaa-Xaa-Arg/Ala) (SEQ ID NO: 9), and a C-terminal domain of 120 amino acids containing the seven highly conserved cysteines characteristic of the TGF- β gene family. See page 10, lines 11-16.

10 Alignment of the carboxy terminal domains of CDMP-1 and -2 with other members of the BMP family revealed an amino acid identity of about 50% with BMP-5, BMP-6 and OP-1 (BMP-7). These results suggested that CDMP-1 and CDMP-2 are members of a new subfamily. See page 10, last full paragraph.

In general, BMPs are dimeric molecules. The dimeric conformation is critical for biological action. BMP monomers are processed to yield the C-terminal mature monomer of 110+ amino acids. See Reddi (31, cited by Applicants) page 13, left column, last full paragraph.

20 Thus, one would expect that an isolated DNA molecule which codes for a protein of the TGF- β family, wherein said protein has chondrogenic activity in vivo, as claimed, would code for a protein that is secreted as a dimer and then cleaved to result in a biologically active carboxy terminal domain of 110+ amino acids, characterized by 7 highly conserved cysteine residues.

25 The claim only sets forth nucleic acid molecules encoding amino acid sequences that are 31 amino acids in length. One skilled in the art would not expect that these 31 amino acid peptides would have chondrogenic activity in vivo because one would expect that an isolated DNA molecule which codes for a protein of the TGF- β family, wherein said protein has chondrogenic activity in vivo, would code for a protein that is secreted as a dimer and then cleaved to result in a biologically active carboxy terminal domain of 110+ amino acids, characterized by 7 highly conserved cysteine residues. No evidence

Art Unit: 1647

has been brought forth that these 31 amino acid peptides would provide a protein that has chondrogenic activity in vivo. In addition, the specification only discloses a single full-length protein (bovine CDMP-2; SEQ ID NO: 14) comprising SEQ ID NO: 24 and a partial peptide (human CDMP-2; SEQ ID NO: 22) that is SEQ ID NO: 24. Thus, the specification only describes a single species of TGF- β family member that comprises SEQ ID NO: 24. The examiner accordingly finds that the species described with particularity are not representative of the genera implied by the minimal structural limitations imposed by the claims, and that the skilled artisan would thus not have recognized that the inventors were in possession of the invention now claimed at the time the application was filed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 27 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10 and 11 of copending Application No. 10379830. Although the conflicting claims are not identical,

Art Unit: 1647

they are not patentably distinct from each other because the present claims are generic to and fully encompass the claims of the co-pending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5

Conclusion

No claims are allowable.

10 ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571)272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

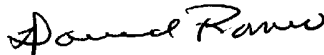
15 BEFORE FINAL (703) 872-9306
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CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

20 ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

25



DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

30

DSR
AUGUST 26, 2004